more oligonucleotide(s) (oligo(s)) effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, bronchoconstriction, allergy(ies) and/or inflammation, and contains up to and including about 15% adenosine (A), the oligo being anti-sense to [the] an initiation codon, [the] a coding region or [the] a 5' or 3' intron-exon junctions of a gene encoding an adenosine A1, A2a, A2b or A3 receptor or anti-sense to their respective mRNA; [combinations of the oligos;] pharmaceutically and veterinarily acceptable salts of the oligo(s) [oligos and their combinations; and mixtures their combinations and their salts and] or mixtures thereof; and

a surfactant [that either counters low levels of natural surfactant or enhances the uptake of the oligo(s) throughout he lung; wherein the surfactant] that may be operatively linked to the nucleic acid.

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109. The composition of claim 108, wherein the oligo consists of up to about 10% A.

110. The composition of claim 109, wherein the oligo consists of up to about 5% A.

111. The composition of claim 110, wherein the oligo consists of up to about 3% A.

112. The composition of claim 111, wherein the oligo is A-free.

113. The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3' intron-exon junctions or to sequences of the coding region comprising 2 or more G and/or C of the adenosine A1 receptor gene.

114. The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3' intron-exon junctions or to sequences of the coding region comprising 2 or more G and/or C of the adenosine A_{2a}, A_{2b} and/or A_3 receptors.

115. The composition of claim 108, wherein if the oligo contains adenosine (A), at least one A is substituted by a universal base selected from the group consisting of heteroaromatic bases which bind to a thymidine base but have antagonist activity and less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} and A_3 receptors, and heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

116. (Amended) The composition of claim 115, wherein substantially all As are substituted by a universal base (s) selected from [the group consisting of] heteroaromatic bases [which] that bind to a thymidine base but either have antagonist activity [and] or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} and A_3 receptors, [and] or heteroaromatic bases [which] that have no activity or have [an] agonist activity at the adenosine A_{2a} receptor.

C2

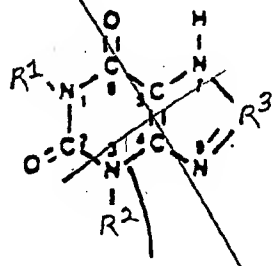
SUB F2 CONT

117. (Amended) The composition of claim 115, wherein the heteroaromatic bases are selected from [the group consisting of] pyrimidines [and] or purines that [, which] may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH [and] or branched [and] or fused primary [and] or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, or arylcycloalkyl, which may be further substituted by O, halo, NH_2, primary, secondary [and] or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl [and] or heteroaryl.

118. The composition of claim 117, wherein the pyrimidines are substituted at a 1, 2, 3, and/or 4 position, and the purines are substituted at a 1, 2, 3, 4, 7 and/or 8 position.

119. (Amended) The composition of claim 118, wherein the pyrimidines [and] or purines are selected from [the group consisting of] theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline [and] or xantine having the chemical formula

SUB. F3



wherein R^1 and R^2 are independently H, alkyl, alkenyl or alkynyl and R^3 is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH_2-alkylamino-ketoxyalkyloxy-aryl [and]

or mono [and] or dialkylaminoalkyl-N-alkylamino-SO_2 aryl.

SUB F3 CONT

120. (Amended0 The composition of claim [119] 116, wherein the universal base is selected from [the group consisting of] 3 – nitropyrrole - 2' - deoxynucleoside, 5 – [nitro-indole] nitroindole, 2' - deoxyribosyl - (5 - nitroindole), 2 – deoxyribofuranosyl - (5 - nitroindole), 2' - deoxyinosine, 2' - deoxynebularine, 6H, 8H - 3, 4 - dihydropyrimido [4, 5 - c] oxazine – 7 - one or 2 – amino – 6 - methoxyaminopurine.

121. The composition of claim 108, wherein a methylated cytosine (^{m}C) is substituted for an unmethylated cytosine (C) in at least one CpG dinucleotide if present in the nucleic acid(s).

122. The composition of claim 108, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

123. (Amended) The composition of claim 122, wherein substantially all mononucleotides are linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-

methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

124. The composition of claim 108, wherein the anti-sense oligo comprises about 7 to 60 mononucleotides.

125. (Amended) The composition of claim 108, wherein the oligo comprises a sequence selected from [the group consisting of] SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 [and] or SEQ ID NO: 7 to [SEQ. ID NO: 1035] SEQ ID NO: 1035, or

SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 1035, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

(Amended) The composition of claim 122, wherein substantially all mononucleotides are linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate,

boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids..

126. The composition of claim 108, wherein the nucleic acid is linked to an agent that enhances cell internalization or up-take and/or a cell targeting agent.

127. The composition of claim 126, wherein the cell internalization or up take enhancing agent is a transferrin, a asialoglycoprotein or a streptavidin.

128. The composition of claim 126, wherein the cell targeting agent comprises a vector, and the nucleic acid is operatively linked to the vector.

129. (Amended) The composition of claim 128, wherein the vector [is] comprises a prokaryotic or eukaryotic vector.

130. (Amended) The composition of claim 108, wherein the surfactant is selected from [the group consisting of] surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D and surfactant protein and active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycero-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic

acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly(vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters and phosphatidyl ethers, palmitates, alcohols and tyloxapol, phospholipids, neutral lipids, fatty acids [and] or surfactant-associated proteins [, and] or $C_{22}H_{19}C_{10}$.

SUB F5 C6 cont

131. (Amended) The composition of claim 130, wherein the the surfactant is selected from [the group consisting of] polyoxy ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), colfoceryl-cetyl alcohol-tyloxapol or colfosceril palmitate, cetyl alcohol, [and] tyloxapol (Exosurf®), phospholipids, neutral lipids, fatty acids, [and] surfactant-associated proteins (Survanta®) [and] or $C_{22}H_{19}C_{10}$ (Atovaquone®).

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~~131.~~ (Amended) The composition of claim 108, which comprises particle sizes of about 0.5 μ to about 10 μ or about 10 μ [0.05] to about 500 μ [m in size of the nucleic acid].

133. (Amended) The composition of claim [132] 108, wherein the carrier comprises a biologically acceptable carrier.

134. The composition of claim 108, wherein the carrier is a pharmaceutically or veterinarily acceptable carrier.

SUB F6 C7

135. (Amended) The composition of claim 134, wherein the carrier is selected from [the group consisting of] gaseous, liquid and solid carriers [and] or mixtures thereof.

136. (Amended) The composition of claim [134] 108, further comprising an agent selected from [the group consisting of] therapeutic agents other than the [oligo] nucleic acid(s), antioxidants, flavoring [and] or coloring agents, fillers, volatile oils, buffering agents, dispersants, RNA inactivating agents, flavoring agents, propellants [and] or preservatives.

SUB F7

137. (Amended) The composition of claim 136, comprising

a pharmaceutically or veterinarily acceptable carrier, [and]

the [a] nucleic acid,

a surfactant, and

a therapeutic agent selected from [the group consisting of] adenosine A_1, A_{2b} [and] or[A_3] receptor activity inhibiting agents other than the oligo(s), anti-arrhythmic agents, anti-inflammatory agents, anti-bacterial agents, anti-sepsis agents, adenosine [and] or agents exhibiting adenosine agonist activity, analgesics, diuretics, kidney activity maintenance [and] or restoration agents [and] or agents for the treatment of pulmonary vasoconstriction, inflammation, allergies, asthma, acute respiratory distress syndrome (ARDS), ischemia, impeded and blocked respiration, respiratory distress syndrome (RDS), pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD) [, cancers selected from the group consisting of melanoma, hepatocellular carcinoma, leukemias, lymphomas and carcinomas of the colon, breast, lung, pancreas, kidney, hepatic, lung, breast and prostate cancer, and metastatic cancers, and to combat side effects produced by radiation agents, chemotherapeutic agents, antibody therapy agents and phototherapeutic agents].

SUB FT cont CT cont

138. The composition of claim 136, wherein the RNA inactivating agent comprises an enzyme.

139. The composition of claim 138, wherein the enzyme comprises a ribozyme.

140 The composition of claim 108, further comprising a propellant.

141. The composition of claim 108, wherein the nucleic acid is present in an amount of about 0.01 to about 99.99 w/w of the composition.

143. (Amended) The formulation of claim [142] 108, selected from [the group consisting of] intrabuccal, intrapulmonary, [intratumor] respirable, nasal, [intravascular,] inhalable, [transdermal,] intracavitary, [implantable, iontophoretic,] intraorgan, [implantable,] or slow release [and enteric coating] formulations.

C8

144. (Amended) The formulation of claim 143, wherein the carrier is selected from [the group consisting of] gaseous, solid [and] or liquid carriers.

146. (Amended) The aerosol formulation of claim [144,] 108, wherein which is selected from [the group consisting of a] powders, [capsules,] sprays, [aerosols,] solutions, suspensions [and] or emulsions.

C9 SUB F8

148. (Amended) The aerosol formulation of claim [143] 108, [wherein the carrier is] selected from [the group consisting of] aqueous [and] or alcoholic solutions [and] or suspensions, oily solutions [and] or suspensions [and] or oil-in-water [and] or

C10

SUB F8 CM 7

water-in-oil emulsions.

151. (Amended) A [n implantable] capsule or cartridge, comprising the formulation of claim 143.

C11

152. (Amended) The aerosol formulation of claim 146, comprising a powdered spray or aerosol

[142, wherein the carrier is selected from the group consisting of aqueous and alcoholic solutions and suspensions, oily solutions and suspensions and oil-in-water and water-in-oil emulsions].

153. (Amended) The formulation of claim [142] 108, wherein the carrier comprises a hydrophobic carrier.

154. The formulation of claim 153, wherein the carrier comprises lipid vesicles and/or particles.

155. The formulation of claim 154, wherein the vesicles comprise liposomes and the particles comprise microcrystals.

C12

156. (Amended) The formulation of claim 155, wherein the vesicles comprise liposomes [which] that comprise the [mucleic] nucleic acid.

C13 SUB F9

158. (Amended) The formulation of claim [157] 143, which is an intrapulmonary, intracavitary or intraorgan liquid or powdered formulation of particle size about 0.5 μ to 10 μ or about 10 μ to 500 μ.

159. (Amended) The formulation of claim [157] 143, which is a nasal formulation of particle size about 10 μ to 500 μ.

161. (Amended) The formulation of claim 143, in bulk, or in single or multiple unit dose form.

C14

162. (Amended) The formulation of claim 143, which is a respirable or inhalable formulation comprising a powdered or liquid aerosol of particle size about 0.5 μ to about 10 μ [in bulk].

163. A cell, comprising the nucleic acid of claim 108.

C15 SUB F10

164. (Amended) A kit for diagnosis or treatment of diseases and conditions associated with hypersensitivity to and/or increased levels of, adenosine and/or bronchoconstriction and/or allergy(ies) and/or inflammation and/or asthma, comprising in separate containers [a]

the delivery device of claim 222;

a nucleic acid comprising at least one oligonucleotide (oligo) effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, or alleviate bronchoconstriction, asthma or lung allergy(ies) and/or inflammation, the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, with bronchoconstriction, asthma, or lung allergy(ies) or inflammation, or being anti-sense to the corresponding mRNA; the nucleic acid comprising one or more oligo(s), their mixtures or their pharmaceutically or veterinarily acceptable salts of the oligo(s) [the composition of claim 108]; and

SUB F10 CONT

instructions for preparation of a respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of particle size about 0.5 to about 500 μ and for its use; and

C 15 CONT

optionally an agent selected from [the group consisting of] therapeutic [and] or diagnostic agents other than the oligo, anti-oxidants, fillers, volatile oils, dispersants, anti-oxidants, flavoring agents, propellants, preservatives, solvents, buffering agents, RNA inactivating agents, [cell-] agents that are internalized [and] or up-taken [agents and] by a cell, or coloring agents.

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165. (Amended) The kit of claim 164, wherein the delivery device comprises a nebulizer [which] that delivers single metered doses of [the] a powdered or liquid aerosol formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ of the nucleic acid.

166. (Amended) The kit of claim [165] 164, wherein the device [nebulizer] comprises an insufflator adapted for receiving and piercing or opening a capsule(s) or cartridge(s) producing a powdered or liquid aerosol; and the nucleic acid [composition] is provided separately in a piercable or openable capsule(s) or cartridge(s) as a nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

SUB F11

167. (Amended) The kit of claim [165] 164, wherein the delivery device comprises a pressurized [inhaler] inhalator that delivers a powdered or liquid aerosol of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ; and the nucleic acid

is provided as [composition comprises] a suspension, solution, emulsion or dry powder aerosol formulation of [the agent] about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

168. (Amended) The kit of claim [167] 164, comprising the delivery device, a surfactant, [a] the nucleic acid and a therapeutic agent selected from [the group consisting of anti-] adenosine A_1, A_{2b} [and] or A_3 receptor antagonists other than the oligo(s), adenosine A_{2a} receptor stimulants, anti-inflammatory agents, anti-histaminic agents, anti-allergic agents, anti-bacterial, anti-vials, analgesics, kidney activity maintenance [and] or restoration agents, anti-cancer agents, adenosine, blood pressure controlling agents, [and] or diuretics.

SUB FII CMT SUB D6

169. (Amended) The kit of claim [167] 164, wherein the solvent is selected from [the group consisting of] organic solvents [and] or organic solvents mixed with one or more co-solvents.

CIS CMT

170. (Amended) The kit of claim 164, wherein the [composition] device is adapted for receiving a capsule(s) or cartridge(s), and the nucleic acid is separately provided as an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation in a capsule(s) or cartridge(s).

SUB Q17

171. (Amended) The kit of claim [163] 164, further comprising in a separate container a propellant and pressurized means for delivery adapted for delivering a powdered or liquid aerosol, [thereof;] and instructions for loading into the delivery device [preparation and delivery of a composition comprising particles of about 0.05 to about 50 μm in size of the nucleic acid] the nucleic acid as an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ, and then joining the device with the propellant and the pressurized means.

SUB FI 2

172. (Amended) The kit of claim 167, wherein the pressurized inhalator further comprises [ing] a propellant and [,] means for delivery [thereof, and instructions for preparation and delivery of a composition] of the propellant, and delivers thenucleic acid as a liquid or powdered aerosol formulation [comprising particles of about 0.05 to about 50 μm in size] of the nucleic acid [with the propellant means].

173. (Amended) An in vivo method of delivering a pharmaceutical composition to a target polynucleotide, comprising administering to the airways of a

subject an aerosol composition of particle size about 0.5 μ to about 500 μ, comprising a nucleic acid which comprises at least one oligonucleotide (oligo) effective to alleviate hyper-responsiveness to, and/or increased levels of, adenosine, or alleviate bronchoconstriction, asthma or lung allergy(ies) and/or inflammation, the oligo containing [and contains] up to and including about 15% adenosine (A), [the oligo] and being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, and/or increased levels of, adenosine, with bronchoconstriction, asthma, or lung allergy(ies) and/or inflammation, or being anti-sense to the [respective] corresponding mRNA; the nucleic acid [combinations] comprising one or more [than one] oligo(s), [;] pharmaceutically and veterinarily acceptable salts of the [nucleic acid] oligo(s), [and] mixtures of the oligo(s) [nucleic acids, their combinations and] or their salts.

175. (Amended) The method of claim [174] 173, wherein the [disease or condition is] hyper-responsiveness to, or increased levels of, adenosine, or bronchoconstriction, asthma or lung allergy(ies) or inflammation is associated with [selected from the group consisting of one or more of] sepsis, pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, acute respiratory distress syndrome (ARDS), renal damage or failure, ischemia, pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD) [, and cancers selected from the group consisting of leukemias, lymphomas and carcinomas of the colon, breast, lung, pancreas, hepatocellular carcinoma, kidney, melanoma, hepatic, lung, breast and prostate cancer, metastatic cancer, and cancers that are or will be treated with treatments selected from radiation, chemotherapeutic, antibody therapy and phototherapeutic agents].

178. (Amended) The method of claim [174] 173, wherein the composition is administered intrapulmonarily, intraorgan, intracavitarily, intrabuccal, intranasally, by inhalation or into the subject's respiratory system.

179 [178]. (Amended) The method of claim [174] 173, wherein the [agent] oligo is effective to reduce hyper-responsiveness to adenosine, the amount of the adenosine receptor or the production or availability of adenosine, or to increase the degradation of the adenosine receptor mRNA.

180 []79]. (Amended) The method of claim [173] 178, wherein the [agent] oligo is administered directly into the subject's lung (s), intraorgan, intracavitarily, intrabuccal or intrapulmonarily.

C17 CONT SUB F13

181 [180]. (Amended) The method of claim [173] 178, wherein the composition [comprises] is administered as powdered solid or liquid particles of the nucleic acid about 0.5 to about 10 μ in size.

SUB F14

183 [184]. (Amended) The method of claim [180] 181, wherein the composition is administered as powdered solid or liquid nucleic acid particles [are] greater than about 10 [to about 500] μ in size.

184 [183]. (Amended) The method of claim 173, wherein the composition further comprises a surfactant

[that enhances the uptake of the nucleic acid(s) throughout he lung].

C18

185 [184]. (Amended) The method of claim 174, wherein the hyper-responsiveness to, and/or increased levels of, adenosine, or bronchoconstriction, asthma or lung allergy(ies) or inflammation [disease or condition] is associated with bronchoconstriction of lung airways.

SUB F15

186 [185]. (Amended) The method of claim [184] 185, wherein the hyper-responsiveness to, or increased levels of, adenosine, or bronchoconstriction, asthma or lung allergy(ies) or inflammation is associated with [disease or condition is selected from the group consisting of] COPD, asthma, ARDS, side effects of adenosine administration [and] or renal damage.

187 [186]. (Amended) The method of claim [174] 173, wherein the hyper-responsiveness to, or increased levels of, adenosine, or bronchoconstriction, asthma or lung allergy(ies) or inflammation [disease or condition] is associated with inflammation or an inflammatory disease.

SUB F15

188 [187]. The method of claim 173, wherein the composition further comprises a therapeutic agent selected from [the group consisting of] adenosine A_1, A_{2b} [and] or A_3 receptor inhibiting agents [and] or adenosine A_{2a} receptor stimulating agents other than the nucleic acid(s), anti-inflammatory agents, anti-bacterial agents, anti-sepsis agents, kidney activity maintenance [and] or restoration agents [and a] or gents for the treatment of pulmonary vasoconstriction, inflammation, allergies, asthma, impeded

respiration, respiratory distress syndrome (RDS), pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD) [, radiation agents, chemotherapeutic agents, antibody therapy agents, phototherapeutic agents, adenosine, anti-arrhythmic agents and cancers selected from hepatocellular carcinoma, leukemias, lymphomas or carcinomas of the colon, breast, lung, pancreas, kidney, melanoma, liver, lung, breast or prostate cancer, or metastatic cancer].

189 [188]. (Amended) The method of claim [187] 188, wherein the therapeutic agent is selected from [the group consisting of] anti-adenosine A_1, A_{2b} [and] or A_3 receptor agents [and] or adenosine A_{2a} receptor stimulating agents [,] other than the nucleic acid(s).

190 [189]. (Amended) The method of claim [188] 189, wherein the disease or condition is associated with sepsis.

191 [190]. (Amended) The method of claim [173] 184, wherein the surfactant is selected from surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D and surfactant protein and active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycero-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, polyoxy ethylene ethers, phenoxy polyethoxy alcohols, phosphatidyl choline esters and phosphatidyl ethers, palmitates, alcohols and tyloxapol, phospholipids, neutral lipids, fatty acids or surfactant-associated proteins, and $C_{22}H_{19}C_{10}$

[composition is administered intracavitarily, intranasally, intrabucally, by inhalation, or intrapulmonarily].

C19 CONT

192 [191]. (Amended) The method of claim 173, wherein the subject is a mammal.

193 [192]. (Amended) The method of claim [191] 192, wherein the mammal is a human or a non-human mammal.

SUB Q26

195 [194]. (Amended) The method of claim 173, wherein the [anti-sense] nucleic acid is administered in amount of about 0.005 to about 150 mg/kg body weight.

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196 [195]. (Amended) The method of claim [194] 195, wherein the [anti-sense] nucleic acid is administered in an amount of about 0.01 to about 75 mg/kg body weight.

197 [196]. (Amended) The method of claim [195] 196, wherein the nucleic acid is administered in an amount of about 1 to about 50 mg/kg body weight.

198 [197]. (Amended) The method of claim 173, which is a prophylactic or therapeutic method.

SUB Q27

200 [199]. (Amended) The method of claim 173, wherein the nucleic acid is obtained by

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(a) selecting fragments of a target nucleic acid having at least 4 contiguous [nucleic acids] bases selected from the group consisting of G and C;

(b) obtaining a first oligo 4 to 60 nucleotide long which comprises the selected fragment and has a C and G nucleic acid content of up to and including about 15%; and

(c) obtaining a second oligo 4 to 60 nucleotide long comprising a sequence which is anti-sense to the selected fragment, the second oligo having an A base content of up to and including about 15%.

201 [200]. (Amended) The method of claim 173, wherein the oligo consists of up to about 10% A.

202 [201]. (Amended) The method of claim [200] 201, wherein the oligo consists of up to about 5% A.

203 [202]. (Amended) The method of claim [200] 201, wherein the oligo consists of up to about 3% A.

204 [203]. (Amended) The method of claim [202] 203, wherein the oligo is A-free.

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205 [204] (Amended) The method of claim 173, wherein the oligo is anti-

sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding an adenosine A1, A2b or A3 receptor and the composition further comprises a surfactant.

206 [205]. (Amended) The method of claim 173, wherein if the oligo contains A_n at least one A is substituted [by] with a universal base selected from [the group consisting of] heteroaromatic bases which bind to a thymidine base but have antagonist activity [and] or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} [and] or A_3 receptors, [and] or heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

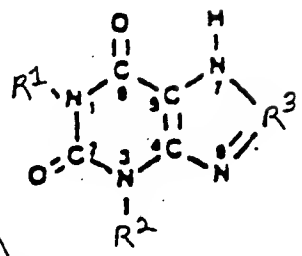
207 [206]. (Amended) The method of claim [205] 206, wherein all As are substituted [by] with universal bases selected from [the group consisting of] heteroaromatic bases which bind to a thymidine base but have antagonist activity [and] or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} [and] or A_3 receptors, [and] heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

208 [207]. (Amended) The method of claim [205] 206, wherein the heteroaromatic bases are selected from [the group consisting of] pyrimidines and purines, which may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH [and] branched [and] fused primary [and] secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, which may be further substituted by O, halo, NH_2, primary, secondary and tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl [and] or heteroaryl.

209 [208]. (Amended) The method of claim [207] 208, wherein the pyrimidines are substituted at positions 1, 2, 3 and\or 4, and the purines are substituted at positions 1, 2, 3, 4, 7 and\or 8.

210 [209]. (Amended) The method of claim [208] 209, wherein the pyrimidines and purines are selected from [the group consisting of] theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline [and]

or xantine having the chemical formula



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wherein R^1 and R^2 are independently H, alkyl, alkenyl or alkynyl and R^3 is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH_2-alkylamino-ketoxyalkyloxy-aryl and mono and dialkylaminoalkyl-N-alkylamino-SO_2 aryl.

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211 [210]. (Amended) The method of claim [209] 206, wherein the universal base is selected from [the group consisting of] 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one or 2-amino-6-methoxyaminopurine.

212 [211]. (Amended) The method of claim 173, further comprising methylating at least one cytosine vicinal to a guanosine into a methylated cytosine [cytosime] (^{m}C) if a CpG dinucleotide if present in the oligo(s).

213 [212]. (Amended) The method of claim 173, further comprising modifying or substituting at least one mononucleotide [linking phosphodiester residue of or modifying] of the anti-sense oligo(s) with methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methyimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues, [and] or combinations thereof.

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214 [213]. (Amended) The method of claim [212] 213, wherein all mononucleotides [phosphodiester residues] are substituted and/or modified.

215 [214]. (Amended) The method of claim 173, further comprising operatively linking the nucleic acid to an agent selected from [the group consisting of] agents that enhance cell internalization or up-take [and] or cell targeting agents.

216 [215]. (Amended) The method of claim [214] 215, wherein the cell

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internalization or up-take enhancing agent is selected from [the group consisting of] transferrin, asialoglycoprotein [and] or streptavidin.

217 [216]. (Amended) The method of claim [214] 215, wherein the cell targeting agent [is] comprises a vector.

218 [217] (Amended) The method of claim [216] 217, wherein the vector to which the agent is operatively linked [is] comprises a prokaryotic or eukaryotic vector.

219 [218]. (Amended) The method of claim 173, wherein the nucleic acid comprises an oligo sequence selected from [the group consisting of] SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 [and] or SEQ ID NO: 7 to [SEQ. ID NO:1035,] SEQ ID NO: 1035, or

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SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO: 7 to SEQ ID NO:1035, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or fatty acids.

Please add the following claims:

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-- 220. The method of claim 191, wherein the the surfactant is selected from [the group consisting of] polyoxy ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), colfoceryl-cetyl alcohol-tyloxapol or colfosceril

but F21 cont

palmitate, cetyl alcohol, [and] tyloxapol (Exosurf®), phospholipids, neutral lipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}C_{10}$ (Atovaquone®).

221. The method of claim 173, wherein the hyper-responsiveness to, or increased levels of, adenosine, or bronchoconstriction, asthma or lung allergy(ies) or inflammation is associated with asthma or a disease or condition associated with asthma.

222. A diagnostic or therapeutic device adapted for delivering a respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of particle size about 0.5 μ to about 500 μ, the formulation comprising a nucleic acid which comprises at least one oligonucleotide (oligo) effective for diagnosing or treating hyper-responsiveness to, or increased levels of, adenosine, or bronchoconstriction, asthma or lung allergy(ies) or inflammation, or a disease or condition associated with either of them, the oligo being anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to, or increased levels of, adenosine, bronchoconstriction, asthma, or lung allergy(ies) or inflammation, or being anti-sense to the corresponding mRNA; the nucleic acid comprising one or more oligo(s), their mixtures, or their pharmaceutically or veterinarily acceptable salts.

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223. The device of claim 222, comprising a nebulizer adapted for delivering single metered doses of the formulation as a powdered or liquid aerosol of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

224. The device of claim 222, which comprises an insufflator adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and for producing a powdered or liquid aerosol of particle size about 0.5μ to about 10 μ or about 10 μ to about 500 μ, and wherein the formulation is provided separately in a piercable or openable capsule(s) or cartridge(s) as a nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ.

225. The device of claim 222, which comprises a pressurized inhalator that delivers a powdered or liquid aerosol of particle size about 0.5 μ to about 10 μ or about 10 μ to about 500 μ; and wherein the formulation comprises a suspension, solution, emulsion or dry powder aerosol formulation of the nucleic acid of particle size about 0.05 μ to about 50 μ or about 10 μ to about 500 μ.

226. The pressurized inhalator of claim 225, further comprising in a separate container a propellant and pressurized means for delivery, adapted for delivering a powdered or liquid aerosol, and instructions for loading into the delivery device the the inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation, and joining the device with the propellant and the pressurized delivery means.

SUB F2) CONT

227. The pressurized inhalator of claim 225, further comprising a propellant and propellant delivery means, wherein the pressurized inhalator delivers the formulation as a liquid or powdered aerosol.

228. The device of claim 222, which is adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and the formulation is provided separately in a capsule(s) or cartridge(s).

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229. The kit of claim 164, wherein the oligo is antisense to the initiation codon, the coding region or the 5' or 3' region of a gene encoding a polypeptide selected from an adenosine A_1 receptor, adenosine A_{2a} receptor, adenosine A_{2b} receptor, adenosine A_3 receptor, IgE receptor β, Fc-epsilon receptor CD23 antigen, IgE receptor α subunit, IgE receptor Fc ϵ R, histidine decarboxylase, beta tryptase, tryptase-I, prostaglandin D synthase, cyclooxygenase-2, eosinophil cationic protein, eosinophil derived neurotoxin, eosinophil peroxidase, P selectin, endothelial monocyte activating factor (IL-3), interleukin-3 (IL-3), interleukin-5 (IL-5), interleukin-6 (IL-6), monocyte-derived neutrophil chemotactic factor, neutrophil elastase (medullasin), neutrophil oxidase factor, cathepsin G, defensin 1, defensin 3, macrophage inflammatory protein-1-α, muscarinic acetylcholine receptor HM1, muscarinic acetylcholine receptor HM3, fibronectin, interleukin-8 (IL-8), GM-CSF, tumor necrosis factor α, leukotriene C4 synthase or major basic protein.

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230. The kit of claim 229, for diagnosis or treatment of sepsis, pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, acute respiratory distress syndrome (ARDS), renal damage or failure, ischemia, pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, emphysema or chronic obstructive pulmonary disease (COPD).

231. The kiy of claim 164, wherein the nucleic acid comprises an oligo